Citation:

Maki KC, Rains TM, Kaden VN, Raneri KR, Davidson MH. Effects of a reduced-glycemic-load diet on body weight, body composition, and cardiovascular disease risk markers in overweight and obese adults. *Am J Clin Nutr.* 2007 Mar; 85(3): 724-734.

PubMed ID: 17344493

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

This randomized controlled trial was designed to evaluate the effects of an ad libitum reduced-glycemic-load (RGL) diet on body weight, body composition and cardiovascular disease (CVD) risk markers in overweight and obese adults during an initial weight-loss phase (12 weeks) and a weight-loss maintenance phase (weeks 24 to 36).

Inclusion Criteria:

- Discontinue all use of dietary supplements or multivitamins and follow assigned diet and maintain their usual level of physical activity throughout the trial
- Men and women aged 18 to 65 years
- Waist circumference measurement at week one of 87cm or more for women and 90cm or more for men
- In good health on the basis of medical history and routine laboratory tests.

Exclusion Criteria:

- A weight loss of more than 4.5kg in the two months before screening, had a body mass index (BMI) of more than 37kg/m^2, were current smokers or had a history of smoking in the six months before screening
- Diagnosis of diabetes mellitus, uncontrolled hypertension or a history of cancer in the past two years
- A history of or current significant cardiac, renal, pulmonary, hepatic, biliary or endocrine disease
- A history of recurrent nephrolithiasis or acute nephrolithiasis within the year before screening
- Use of any weight-loss medication, supplements, programs, or meal-replacement products

intended to alter body weight during the four weeks before screening or if they had any diagnosed eating disorder, a history of surgery for weight-reducing purposes or a clinically significant gastrointestinal disorder
- Use of systemic corticosteroids, androgens, phenytoin or pseudoephedrine; lipid-lowering therapies (unless dose-stable for two months before enrollment); drugs for regulating hemostasis other than dose-stable aspirin; thyroid hormones (except stable-dose replacement therapy)
- Post-menopausal women who were current users of sex hormone therapy or who had discontinued use in the two months before screening.
- Female subjects who were pregnant, planning to be pregnant during the study period or lactating, or those of childbearing potential who were not using an approved method of contraception.

Description of Study Protocol:

Recruitment

Potential participants were recruited from the Chicago metropolitan area and screened by telephone.

Design

- A randomized, controlled design with two parallel treatment arms
- Subjects were randomly assigned to either the RGL or portion-controlled (control) diet. Weeks zero to 12 were weight-loss treatment. At some point between weeks 12 and 24, each subject transitioned to a weight-maintenance phase. From week 24 on, all subjects were in the weight-maintenance phase.

Dietary Intake/Dietary Assessment Methodology

- Diet counselors were the same for both groups. Diet training manuals were created to standardize training of the counselors. All were Registered Dietitians (RD) with extensive experience in counseling for weight management
- For both diet groups, handouts were provided to each subject for at-home use and dietary guidance was reinforced at each treatment visit
- For subjects assigned to the control diet, energy needs for weight maintenance were estimated from basal EE calculated with the Harris-Benedict equation multiplied by an activity factor of 1.2, 1.3 or 1.4 after evaluation of activity level from the results of the Stanford seven-day physical activity questionnaire
- On the basis of a review of diet records returned, recommendations were made on substitutions for high-fat foods and decreasing portion sizes and energy density to produce a target energy deficit of 500 to 800kcal per day, while consuming a nutritionally balanced diet
- Subjects were encouraged to achieve weight loss of approximately 0.5kg per week
- Those following the RGL diet were instructed to eat three meals a day plus snacks and to eat until hunger was satisfied. Specific high-carbohydrate foods, including all starchy foods and fruits, were eliminated during phase 1 of the diet (the first two weeks)
- Subjects were advised not to consume any alcohol during this period and were instructed on selection of foods with low carbohydrate content that are not high in saturated fat and trans fats to avoid excessive intake of cholesterol-raising fatty acids. At week two, subjects received instructions for the second phase of the diet.

Intervention

- Subjects were assigned to RGL (N=43) or low fat, portion-controlled (control, N=43) groups. The RGL group was instructed to eat until satisfied, maintaining a low carbohydrate intake during weeks zero to two and adding low glycemic index carbohydrate thereafter
- Control subjects were instructed to reduce fat intake and decrease portion sizes, with a targeted energy deficit of 500 to 800kcal per day.

Statistical Analysis

- Statistical analyses were conducted with SAS software (versions 8.02 and 9.1; SAS Institute, Cary, NC). All tests of statistical significance were performed at alpha 0.05, two-sided, unless otherwise indicated
- The Shapiro-Wilk test (25) was used to test variables for normality. Where necessary because of non-normality, rank transformations were employed before calculation of inferential statistics
- Baseline comparability of treatment groups was assessed by one-factor analysis of variance (ANOVA) for continuous variables and chi-square or Fisher's exact test for categorical variables
- An intent-to-treat analysis of outcome variables was completed by using all data for subjects with body weight measurement
- For this analysis, which was considered primary, the last non-baseline observation was carried forward for missing data points. A secondary analysis for body weight was also completed, in which the baseline weight was substituted after discontinuation for all subjects who dropped out during the treatment period.
- Additionally, analyses were completed that excluded subjects who did not complete the 36-week study or who violated the protocol in some material way
- For all continuous variables, repeated-measures ANOVA models were employed for values at baseline and weeks two (dietary variables only), 12 and 36. These models each included terms for treatment, time and treatment time interaction. Pair-wise comparisons between groups were completed for individual time points when the treatment time interaction term was significant (P=0.05) in the repeated-measures model
- Body weight responses at weeks 12 and 36 were considered the primary outcome variables and were assessed by ANOVA, with baseline body weight and treatment group as factors in the model. For both the primary and secondary body weight response analyses, the P-values obtained at weeks 12 and 36 were adjusted (multiplied by 1.724) to account for the two comparisons (26). This adjustment equated to the requirement of a nominal, two-sided P-value of 0.029 to obtain statistical significance.

Data Collection Summary:

Timing of Measurements

- 15 clinic visits: One screening visit (week one), one visit at baseline (week zero), seven visits during the weight-loss treatment phase (weeks one, two, four, six, eight, 10 and 12), three visits during the transition from weight-loss treatment to weight-loss maintenance (weeks 16, 20 and 24) and three visits during the weight-loss maintenance phase (weeks 28, 32 and 36)
- Visits were conducted between 7:00 a.m. and 12:00 noon.

Dependent Variables

- Body weight
- Body composition: Fat mass and fat-free mass values measured using HOLOGIC SYSTEMS software
- Cardiovascular disease risk markers.

Independent Variables

An ad libitum reduced-glycemic-load (RGL) diet.

Description of Actual Data Sample:

- *Initial N:* 122
- *Attrition (final N):* 86
    - *RGL group:* 29 women, 14 men
    - *Control group:* 29 women, 14 men
- *Age:*
    - *RGL group:* 47.9±1.8 years
    - *Control group:* 51.4±1.5 years
- *Ethnicity:*
    - *Non-Hispanic white:*
        - *RGL group:* 19%
        - *Control group:* 26%
    - *African American:*
        - *RGL group:* 15%
        - *Control group:* 15%
    - *Hispanic:*
        - *RGL group:* 6%
        - *Control group:* 1%
    - *Other:*
        - *RGL group:* 3%
        - *Control group:* 1%
- *Anthropometrics:* BMI:
    - *RGL group:* 32.1±0.6kg/m^2
    - *Control group:* 31.6±0.5kg/m^2
- *Location:* Chicago metropolitan area.

Summary of Results:

Key Findings

- The RGL group had lost significantly more weight than control group at week 12 (4.9 and 2.5kg, respectively; P=0.002), but the two groups did not differ significantly at week 36 (4.5 and 2.6kg, respectively; between the groups at week 12 (1.9 and 0.9kg, respectively; P=0.016) but not at week 36 (2.0 and 1.3kg, respectively; P=0.333)
- At the end of the study, no differences were found in responses for CVD risk markers except a larger mean change in HDL-cholesterol in the RGL group than in the control group (3.8 and 1.9mg per dL, respectively; P= 0.037).

Author Conclusion:

- In free-living, overweight and obese subjects, an ad libitum RGL diet produced greater losses of body weight and fat than did a traditional, portion-controlled diet during an initial weight-loss period
- Weight regain from the point of maximal weight loss did not differ between treatments. However, the differences in body weight and body fat responses between groups were no longer significant at the end of the weight-maintenance phase of the trial (week 36)
- There was no evidence of any adverse effects of the RGL diet on CVD risk factors
- The results suggest that an ad libitum RGL diet is a reasonable alternative to a low-fat, portion-controlled weight-loss diet.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes

2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	Yes
5.	**Was blinding used to prevent introduction of bias?**	Yes

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	N/A
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes

7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	???